REMARKS

In the Office Action dated September 17, 2008, claim 22 was examined while claims 1-21 and 23-39 were withdrawn from further consideration. The Examiner rejected claim 22, and made the rejection final. In response, applicant has the following comments, and in view thereof, respectfully requests reconsideration of pending claim 22.

In the Office Action, claim 22 was rejected under 35 U.S.C. §103(a) as being unpatentable over DeLuca et al U.S. 6,114,317. The Examiner states that the '317 patent teaches a method of modifying or altering the structure of vitamin D compounds to increase its biological activity. The Examiner indicates that the presently claimed compound of claim 22 is broadly encompassed by the genus of the formula set forth at the top of column 5 of the '317 patent when one selects various substituents from a list of alternatives given in the '317 reference for placement at specific sites on the generic chemical formula disclosed in the '317 reference to arrive at applicant's compound as claimed in claim 22 herein. In addition, the Examiner states that the '317 patent exemplifies an embodiment illustrated at the top of column 12 of the '317 reference that is closely related to the currently claimed compound set forth in claim 22 herein. Accordingly, the Examiner believes it would be obvious to one of ordinary skill in the art to select the currently claimed compound of claim 22 since of one ordinary skill in the art would expect it to posses increased biological activity, as taught in the '317 reference.

This identical rejection was made in the previous, non-final Office Action dated January 4, 2007. In response to that first Office Action, the applicant filed an Amendment dated May 4, 2007 arguing that one of ordinary skill in the art would not have selected the compound of claim 22 herein from the huge number of compounds encompassed by the generic formula disclosed in the '317 reference because the presently claimed compound has less binding activity to the vitamin D receptor (VDR). In other words, the applicant argued that there was no motivation for a person of ordinary skill in the art to select and make the compound of claim 22 because its properties are different from the properties of the

compounds set forth in the '317 reference, and thus results in the compound having unexpected properties.

In the current Office Action of September 17, 2008, the Examiner stated that such a response/arguments "fail to comply with 37 CFR 1.111(b) because they amount to a general allegation that the claims define a patentable invention without specifically pointing out how the language of the claims patentably distinguishes them from the references." Applicant respectfully disagrees with the Examiner's statement that applicant's previous reply was "a general allegation" regarding patentability "without specifically pointing out how the language of the claims patentably distinguishes" from the '317 reference cited. Present claim 22 claims a vitamin D analog utilizing its chemical nomenclature together with the structural formula that represents the compound. Thus, the only "language" in claim 22 that could be utilized to patentably distinguish it from the '317 reference is the specific substituents located at specific sites on the chemical formula per se. Thus, the only way to point out how the "language" of claim 22 patentably distinguishes it from the reference is to argue differences in substituents on the chemical formula and/or argue the properties and utilities of the compound because, as the Examiner knows, a compound and all of its properties are inseparable.

With regard to the structure of the compound in claim 22, the Examiner states in the Office Action of September 17, 2008 that "the applicant's have not argued against the fact that the compound is broadly disclosed in the prior art, only a motivation for choosing the claim compound based upon increased/decreased biological activity." The Examiner also states at the top of page 3 that "the applicant's have not argued that the compound is not disclosed" in the prior art. Apparently, although the Examiner must surely recognize that the compound of present claim 22 is not specifically disclosed in the '317 reference, i.e. not specifically named or illustrated therein, the Examiner was expecting applicant to argue that the compound of claim 22 is not "encompassed" by the generic formula in the '317 patent. Applicant clearly cannot do that because when the substituents of formula I in the '317 patent are as indicated by the Examiner, it is apparent that the compound of claim 22 is in fact

encompassed by formula I. In other words, formula I is a generic chemical formula which encompasses a huge number of vitamin D compounds, which by chance also encompasses the presently claimed species of claim 22. It would be fruitless to argue that claim 22 is not a species of the generic chemical formula disclosed in the '317 reference because, in fact, it is encompassed by that generic chemical formula. In that sense, it is true that the compound of present claim 22 is "broadly disclosed" as stated by the Examiner, but it is just as true that the compound of present claim 22 is not specifically disclosed in the '317 reference as stated by Applicant. What is important is that the compound of present claim 22 is not specifically disclosed in the '317 reference, i.e. the compound of present claim 22 is neither named nor specifically illustrated via a chemical structure in the '317 reference. Since the Examiner rejected claim 22 under §103, and not §102, Applicant argued the key issue of whether one of ordinary skill in the art would have been motivated to select the compound of claim 22 from the genus illustrated by formula I in the '317 reference. Thus, the fact that applicant did not argue that the compound of claim 22 is not broadly disclosed or not encompassed by formula I in the '317 reference does not make the response filed May 4, 2007 a failure to comply with 37 CFR 1.111(b).

In view of the latest Office Action, it is clear that the Examiner understands that the present case is a genus-species situation. As the Examiner knows, a generic claim cannot be allowed to an applicant if the prior art discloses a species falling within the claimed genus. However, the opposite situation is not always true. In other words, a genus does not always anticipate a claim to a species within the genus unless the species is clearly named and/or illustrated in the reference. When the compound is not specifically named, but instead it is necessary to select portions of teachings within a reference and combine them, e.g. select various substituents from a list of alternatives given for placement at specific sites on a generic chemical formula to arrive at a specific compound and/or composition, anticipation can only be found if the classes of substituents are sufficiently limited or well delineated. In other words, if one of ordinary skill in the art is able to "at once envisage" a specific compound within the generic chemical formula, the compound is anticipated. Applicant

refers the Examiner to MPEP §2131.02. Under the present circumstances, it is clear that the compound of claim 22 is not specifically named or illustrated in the '317 reference. Further, in view of the various number of substituents needed to be selected, and in view of the vast number of compounds encompassed by the generic formula I in the '317 reference, it is clear that one skilled in the art would not be able to "at once envisage" all of the compounds covered by formula I, and especially the specific compound of claim 22. Thus, in applicant's opinion, the Examiner correctly rejected the claim under 35 USC §103 and not 35 USC §102.

Applicant refers the Examiner to MPEP §2144.08 for a discussion of the obviousness of a species when the prior art teaches a genus. Applicant believes these guidelines in the MPEP are what controls this current genus-species situation because a single prior art reference, i.e. the '317 reference, discloses a genus encompassing the claimed species but does not expressly and/or specifically disclose the particular claimed species. Thus, one skilled in the art could not "at once envisage" the specific compound of claim 22.

In order to establish a *prima facie* case of obviousness in a genus-species chemical composition situation, the Examiner must: (1) determine the scope and contents of the prior art; (2) ascertain the differences between the prior art and the claims in issue; (3) determine the level of skill in the pertinent art; and (4) evaluate any evidence of secondary considerations. The Examiner performed that analysis and has rejected claim 22 under 35 USC §103(a) as being unpatentable over DeLuca et al U.S. 6,114,317. However, in order to establish a *prima facie* case of obviousness in a genus-species chemical composition situation, it is essential that the Examiner find some motivation or suggestion to make the claimed invention in light of the prior art teachings. See MPEP §2144.08(II)(A). How is this motivation or suggestion to make the claimed invention established? Under MPEP §2144.08(II)(A)(4), the Examiner should (a) consider the size of the prior art genus; (b) consider the express teachings of the prior art; (c) consider the teachings of structural similarities in the prior art; (d) consider the teachings of similar properties or uses; (e) consider the predictability of the technology; and (f) consider any other teaching to support

the selection of the species or subgenus. Applicant will now discuss each of these tests for finding "motivation or suggestion" to make the claimed invention of claim 22.

With regard to the size of the genus, in the present situation the generic formula found in the '317 reference covers a vast number of compounds. The Examiner can see that generic formula I may be substituted from a very large list of alternatives given the placement at specific sites on the generic chemical formula, i.e. the substituents Y_1, Y_2, Y_3, Y_4, Y_5, Y_6, Y_7 and Y_8 may be selected from a huge number of alternatives at positions 1, 2, 3, 4, and 10 of the A ring. In addition, the side chain designated by the substituent R encompasses saturated or unsaturated hydrocarbon radicals of 1 to 35 carbon atoms that may be straight chain, branched or cyclic and that may be substituted at one or more locations along the side chain by hydroxy, protected hydroxy, fluro, carbonyl, ester, epoxy, amino or other heteroatomic groups. Applicant refers the Examiner to column 5, lines 20-60 for the various definitions of the substituents Y_1 through Y_8 and to column 5, line 61 through column 6, line 44 for a definition of the numerous configurations for side chain R. Thus, it is clear that generic formula I of the '317 reference covers a huge number of compounds. Thus, this is not a situation where a prior art genus discloses only a small recognizable class of compounds with common properties. See the discussion relating to In re Petering found in MPEP §2144.08(II)(A)(4)(a).

The Examiner seems to point toward the disclosure found at column 12, lines 3-30 of the '317 reference for an exemplification of "related compounds" to the currently claimed compound "with the difference being the presence of a 10ß-substituent (U) which can be a methyl group etc..." Although the structures illustrated at column 12, lines 3-30 are more limited than generic structure I found in the '317 reference, the structures covered by the formulae containing a 10ß-substitution at column 12, lines 3-30 still cover a vast array of compounds. The Examiner should note that the definition of U is found at column 9, lines 50-64. U may be selected from the group consisting of a methyl, a substituted methyl group, an amino group, a substituted amino group, a phosphino group, a substituted phosphino group, an alkyl-sulfinyl group, an aryl-sulfinyl group, an akyl-sulfonyl group, an aryl-

sulfonyl group and aryl with the substituted substituent selected from hydrogen, alkyl, hydroxyalkyl, aminoalkyl, halogenalkyl, alkoxyalkyl, aryloxyalkyl, aryl, halogen, hydroxyl, protected hydroxy, alkoxyl, aryloxyl, acyl, an amino group, an amino group substituted with alkyl or aryl substituents and an oxo group or a cyclic group having 2-5 carbon atoms. In addition, the formulae illustrated containing the 10ß-susbstitution also requires the substitution of a side chain R attached to the CD ring thereof. Thus, all of the side chains defined in the '317 reference at column 5, line 61 through column 6, line 44 are also covered by the 10ß-substitution structures illustrated at column 12, lines 3-30 of the '317 reference. Obviously, the 10ß-substituted compounds illustrated by the formulae at column 12, lines 3-30 cover a huge number of compounds. One cannot say that a person skilled in the art would "immediately invisage each member" of the genus as required by the In re Petering case. One cannot say that the '317 reference described to those with ordinary skill in the art each of the various permutations involved and illustrated by the generic formulae therein "as fully as if he had drawn each structural formula or had written each name", as was the ruling in In re Petering.

It is also important to note that the 10ß-substitution formulae found at column 12 of the '317 reference does not encompass the compound of present claim 22. The compound of claim 22 is a 19-nor vitamin D compound, i.e. has two hydrogen atoms attached to carbon 10 of the A ring. In contrast, the substituent U can not be a hydrogen atom.

The next issue surrounding motivation to select the specific compound of present claim 22, is for the Examiner to consider the express teachings in the '317 reference. If the prior art '317 reference expressly teaches a particular reason to select the claimed species or subgenus, then this supports a prima facie case of obviousness. An express teaching may be based on a statement in the '317 reference such as an art recognized equivalence, or an express teaching of a "preferred" compound. In the present circumstances, there is nothing in the '317 reference which teaches one skilled in the art to select from the vast number of compounds encompassed by formula I a compound where Y_1, Y_2, Y_3, Y_4, Y_7 and Y_8 are all hydrogen, where Y_5 and Y_6 must be taken together to represent a methylene group, and R is

the 20(S) saturated side chain having 6 carbon atoms with 2 methyl groups and a hydrogen atom attached to the carbon 25 of the side chain. The Examiner can point to no express teachings found in the '317 reference which would direct a person skilled in the art to select that particular combination of substituents from all of the compounds covered by formula I. The only express teaching found in the '317 reference is to choose a substituent which would drive the vitamin D nucleus into the inverted A ring chair conformation with the 1α hydroxyl group in its axial orientation. There is nothing, however, which correlates that teaching to selecting all of the substituents in order to obtain the compound of present claim 22.

The next issue surrounding motivation is for the Examiner to consider the teachings of structural similarities. In other words, the Examiner should consider any teachings of a "typical", "preferred", or "optimum" species or subgenus within the disclosed genus. If such a species or subgenus is structurally similar to the compound claimed, its disclosure may motivate one of ordinary skill in the art to choose the claimed species or subgenus from the genus, based on the reasonable expectation that structurally similar species usually have similar properties. See MPEP §2144.08(II)(A)(4)(c). The Examiner points to the 10ß-substitution compounds found at column 12 of the '317 reference for a teaching of structural similarity. However, Applicant has already indicated that the formulae covering the 10ß-substitution encompasses a vast array of vitamin D compounds. In addition, it is important to note that the definition of "U" does not encompass the presently claimed compound of claim 22. The compound of claim 22 requires two hydrogen atoms attached to the 10 position of the A ring which results in the compound being a "19-nor" vitamin D compound. The Examiner should note that none of the structural formulae set forth at column 12 of the '317 reference covers a 19-nor vitamin D compound. The definition of U found at column 9, lines 50-64 does not include U being a hydrogen atom. This is because the teaching of the '317 reference is for U to be selected from a group of fairly large substituents so as to drive the vitamin D nucleus into the inverted A-ring chair conformer wherein the group U interacts with the 1α hydroxyl group to drive the 1α hydroxyl group into its axial orientation. Thus, the definition of U does not encompass hydrogen because a hydrogen atom is not large

enough to interact with the hydroxyl group in the 1 position to drive the hydroxyl group into its axial orientation. Thus, it is believed one skilled in the art would recognize that U being a hydrogen atom would not be desirable, and would further recognize that is why the definition of U does not include a hydrogen atom. Thus, instead of directing one skilled in the art to U being hydrogen, the '317 reference appears to direct one skilled in the art to groups larger than hydrogen. To Applicant, it thus appears that the '317 reference teaches away from U being defined as a hydrogen atom.

The next issue surrounding motivation is for the Examiner to consider the teachings of similar properties or uses in the prior art. It is the properties and utilities that provide real world motivation for a person of ordinary skill to make species structurally similar to those in the prior art. See MPEP §2144.08(II)(A)(4)(d). In the '317 reference, it is taught that the inverted A ring chair conformer is favored having a 1α hydroxyl group in the axial orientation, and if the compound has its 1α hydroxyl group in an axial position, the greater the biological response that can be expected. See column 3, line 57 through column 4, line 19, especially lines 3-5 of the '317 reference. In contrast, the biological activity of the compound in claim 22 has less binding activity to the VDR than the natural hormone 1α,25-dihydroxyvitamin D_3. Applicant refers the Examiner to the Remarks section of the previous Amendment dated May 4, 2007 wherein Applicant explained that the presently claimed compound of claim 22 does not have increased biological activity as compared to 1α,25-dihydroxyvitamin D_3 in contrast to the teaching in the '317 reference that it is desirable to have greater biological activity for compounds having their 1α hydroxyl in the axial orientation. Thus, once again, Applicant's position is that one of ordinary skill in the art would not have selected the claimed compound from all of those compounds disclosed in the '317 reference because the '317 reference teaches that increased biological activity is desired whereas the compound of claim 22 has significantly less activity, as it relates to binding to the VDR. The Examiner responds by saying that the activity against VDR is only one example of increased/decreased biological activity and other factors such as solubility, toxicity, etc. factor into biological activity. Although that may be true, one must look at what

is taught in the '317 reference compared to what is taught in the present application when considering whether a person skilled in the art would select the compound of claim 22 from all of the vast number of compounds disclosed in the '317 reference. Under this totality of circumstances test, the '317 reference says it wants vitamin D compounds having increased activity, yet the vitamin D compound claimed by Applicant in claim 22 has decreased biological activity, as it relates to VDR binding. There is no teaching in the '317 reference regarding the Examiner's position regarding "other factors", and thus on its face, Applicant's compound would not be desirable in view of what is taught in the '317 reference.

The next issue surrounding motivation is for the Examiner to consider the predictability of the technology. If the technology is unpredictable, it is less likely that structurally similar species will render a claimed species obvious because it may not be reasonable to infer that they would share similar properties. See MPEP §2144.08(II)(A)(4)(e). As stated in the MPEP, obviousness does not require absolute predictability, only a reasonable expectation of success, i.e. a reasonable expectation of obtaining similar properties. However, in the present circumstances, Applicant has demonstrated that the properties of the compound of claim 22 and the desirable properties of the compounds in the '317 reference are dissimilar. The '317 reference wants increased activity, whereas the compound of claim 22 has decreased VDR binding activity. Under the Examiner's theory, one would expect the compound of claim 22 to have increased biological activity, especially binding activity to the VDR, because it is structurally similar to the compounds taught in the '317 reference. However, just the opposite is true, i.e. it has less binding activity than 1α,25-dihydroxyvitamin D_3 which is a result directly opposite of what is desired in the '317 reference.

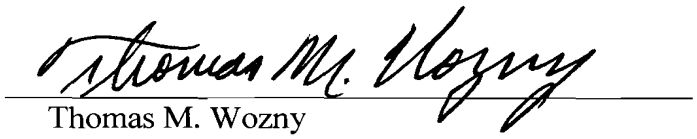
The final issue surrounding motivation is for the Examiner to consider any other teaching to support the selection of the species or subspecies, i.e. the totality of the evidence in each case. See MPEP §2144.08(II)(A)(4)(f). The Examiner has pointed to no other relevant teachings to support the selection of the compound of present claim 22 from the huge number of compounds covered by the generic formula I found in the '317 reference.

The Examiner appears to believe that the prior art '317 reference teaches the identical chemical structure as Applicant's claimed compound of claim 22. However, as noted herein, the '317 reference does not specifically disclose the compound of claim 33. At best, the '317 reference discloses a broad generic chemical formula which encompasses Applicant's compound. However, absent specifically naming and/or illustrating the compound, anticipation cannot be found, but only obviousness. However, Applicant believes it has refuted the prima facie case of obviousness set forth by the Examiner in view of the above analysis.

As a result, Applicant believes claim 22 is now patentable over the '317 reference.

Respectfully submitted,

ANDRUS, SCEALES, STARKE & SAWALL, LLP

By 

Thomas M. Wozny
Reg. No. 28,922

Andrus, Sceales, Starke & Sawall, LLP
100 East Wisconsin Avenue, Suite 1100
Milwaukee, Wisconsin 53202
Telephone: (414) 271-7590
Facsimile: (414) 271-5770